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THE CORRELATION OF SOME HORMONES WITH *ACNE VULGARIS*

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ABSTRACT
Acne vulgaris is a chronic inflammatory skin condition common in adolescence, but occasionally occurs intermittently throughout life. It is characterized by skin eruption on the face, chest, neck and back. In this work seventy-three individuals with acne vulgaris classified into 3 groups, 24 patients with mild acne, 19 patients with moderate acne and 30 patients with severe acne were studied. In addition, included forty-two healthy individuals considered as a control group. The results showed that the testosterone hormone is increased in the patients with Acne vulgaris in both genders but other hormones like FSH & LH showed no significant change between patients and the control group. Only the FSH/LH ratio showed a significant increase in female patients with severe form of acne by comparison with female control group.

KEYWORDS: *Acne Vulgaris*, Hormones, Lipid

INTRODUCTION

Acne is a disorder resulting from the effect of hormones and other substances on the oil glands (sebaceous glands) and hair follicles present in the skin. These factors lead to plugged pores and outbreaks of lesions commonly called pimples or zits. Acne lesions usually occur on the face, neck, back, chest, and shoulders. Although acne is usually not a serious health threat, it can be a source of significant emotional distress. Severe type of acne can lead to permanent scarring.[1] People with acne frequently have a variety of lesions, some of which are shown in the diagrams below figure(1). The basic acne lesion, called the comedone (KOM-e-do), is simply an enlarged and plugged hair follicle. If the plugged follicle, or comedone, stays beneath the skin, it is called a closed comedone and produces a white bump called a whitehead [2]. A comedone that reaches the surface of the skin and opens up is called an open comedone or blackhead because it looks black on the skin's surface. This black discoloration is due to changes in sebum as it is exposed to air. It is not due to dirt. Both whiteheads and blackheads may stay in the skin for a long time.[3]

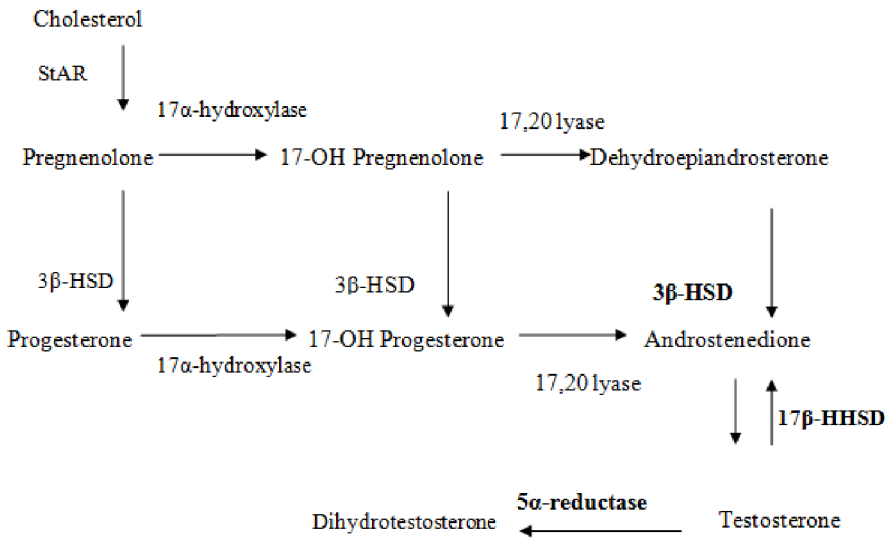

FIGURE-1. The steroidogenic pathway [24]

Hormonal Changes in Acne Vulgaris

With the onset of puberty, the human body starts to produce hormones called androgens or male sex hormones, increasing in both boys and girls. These androgens cause the enlargement and over stimulation of the sebaceous glands which are found in the hair follicles or pores of the skin [4]. The extra sebum or oil that produces by the sebaceous glands mixes with dead skin cells and bacteria on the skin's surface

and this blocks pores. Within the blocked pore, bacteria multiply and cause inflammation. All of this leads to the lesions that are associated with acne. [5]

Teenagers are the most common suffers of acne, purely because of the hormonal shifts that are associated with puberty. Current figures indicate nearly 85% of people will develop acne at some point between the ages of 12 and 25 years. [6]

It is also important to note that the hormonal changes associated with both the menstrual cycle, pregnancy, and even menopause have been shown to be culprits in the creation of acne. Also, when women are either beginning or ending their usage of birth control, the hormonal fluctuations that can occur at this time can cause acne in some women [7].

Relationship between Hormone and Acne

For most people, acne begins at puberty the body starts to produce hormones called androgens. Androgens cause the enlargement and over-stimulation of the sebaceous glands in people with acne. This leads to the overproduction of sebum, and coupled with a sluggish exfoliation process leads to blocked pores and acne. Sensitivity to these androgens also causes acne during the menstrual cycle and sometimes in pregnancy or during the menopause. It's important to note that acne is not caused by excess in hormone levels, but an abnormal reaction to normal levels of these hormones [8].

The acne disease developing in adulthood more than other people; possible reasons for this are diet, lifestyle and more synthetic hormones in our environment (foods, water, plastics and medication). [9]

1. Study the role of some hormonal changes through the study of testosterone level in sera of patients with acne vulgaris compared to control group.
2. Study the role of gonadotropines hormone through study the level of LH & FSH and study the changes in (LH/FSH) ratio in sera of patients with acne vulgaris compared to control groups.

MATERIALS AND METHODS

Subject

Patients

The study was conducted in Hilla city, from December 2008 to September 2009.

Seventy three patients [38 males with mean age $\pm$ SD (20 $\pm$ 4)years and 35 females with mean age $\pm$ SD (20 $\pm$ 2.8) years] with Acne vulgaris, whom were collected from Merjan Teaching Hospital in Hilla city, have been subjected to present study and these selected patients were divided into three groups according to type of disease :-

- The first group includes 24 patients with mild acne vulgaris
- The second group includes 19 patients with moderate acne vulgaris
- The third groups include 30 patients with severe acne vulgaris

Worthy to mention that those patients were not suffering from any other serious systemic illnesses like diabetes mellitus, drug-induced acne, hair-ablation acne ,cardiac, renal and hepatic diseases so as not to interfere with the measured parameters and the outcome of the study.

The control group includes forty-one apparently healthy individuals, after having been asked about their health. PCOS female have been excluded from the control group. Those were divided into two groups:-

– The first one includes 22 females with mean age $\pm$ SD (18 $\pm$ 2.1) years.
– The second one includes 19 males with mean age $\pm$ SD (20$\pm$ 2.6) years.

Testosterone Enzyme Immunoassay Test Kit

– Testosterone hormone was measured by testosterone enzyme immunoassay (ELISA) test kit.

Luteinizing hormone (LH) enzyme immunoassay test kit

– Luteinizing hormone was measured by testosterone enzyme immunoassay (ELISA) test kit.

Follicle Stimulating Hormone (FSH) enzyme immunoassay test kit

– Follicle Stimulating hormone was measured by testosterone enzyme immunoassay (ELISA) test kit.

Statistical analysis

This study is a case – control study. Student's *t*-test has been used to determine the significant difference between two groups, p values less than 0.05 is considered significant.

RESULTS & DISCUSSIONS

Testosterone

The mean serum level of testosterone concentration was significantly higher in patient with acne vulgaris in both genders compared with female and male control groups as shown in table (1). Also serum testosterone was significantly higher in moderate acne and in severe acne patients compared with control group in both genders, while the serum testosterone level shows no significant difference in female with mild acne disease when compared with female control group. Male with mild acne vulgaris shows significant increase in serum testosterone level when compared with control male group as shown in the table (2).

TABLE-1. The Mean Serum Levels of Testosterone in Female & Male in Patients and Control

Testosterone (ng/ml)	Female				Male			
	M *	SD **	No.	p-value	M	SD	No.	P-value
patients	1.6	0.813	35	0.008	11	3.23	38	0.033
control	0.8	0.702	22		10	2.45	19	

* Mean
** Standard deviation

TABLE-2. The Mean Serum Levels of Testosterone in Female & Male in Patients and Control

Female	severe				moderate				mild			
Testosterone (ng/ml)	M	SD	No.	P-value	M	SD	No.	P-value	M	SD	No.	P-value
patients	2.5	2.02	10	0.03	1.65	1.70	11	0.04	0.85	0.39	14	0.15
control	0.8	0.70	22		0.8	0.70	22		0.8	0.70	22	
Male	severe				moderate				mild			
Testosterone (ng/ml)	M	SD	No.	P-value	M	SD	No.	P-value	M	SD	No.	P-value
patients	12.7	3.86	20	0.00	11.7	2.48	8	0.04	11.5	2.51	10	0.03
control	10	2.45	19		10	2.45	19		10	2.45	19	

In this work the elevation of serum testosterone can be attributed to the locally produced androgens and testosterone [10] . The skin and sebaceous gland are capable of producing and metabolizing androgens [11] in addition to producing by adrenal precursor hormone dehydroepiandrostero (DHEAs) [12]. It circulates in the blood stream in relatively high levels compared with other hormones. The main androgens that interact with the androgen receptor are testosterone and DHT. Androgen receptors are found in the basal layer of the sebaceous gland and the outer root sheath keratinocytes of the hair follicle [13] [14].

An essential role for androgens in stimulating sebum production is supported by several lines of evidence. For example, the development of acne in the prepubertal period has been associated with elevated serum levels of DHEAS, a precursor for testosterone [15] [16]. Systemic administration of testosterone and dehydroepiandrosterone increase the size and secretion of sebaceous glands [17], and we know that severe acne is often associated with elevated serum androgens [18] [19] .

The enzyme 3β-hydroxysteroid dehydrogenase (3β-HSD) acts on DHEA to convert it to androstenedione (Fig. 1). This conversion may take place in the adrenal gland and tissues such as the sebaceous gland, where activity of the 3β-HSD enzyme has been identified by several investigators. The reversible conversion of androstenedione into testosterone is then catalyzed in the human skin by 17β-HSD, a member of the short chain alcohol dehydrogenases are related to retinol metabolizing enzymes. [20] [21]

This is a reversible enzyme that can oxidize and reduce both androgens and estrogens. It is responsible for converting the weak androgen androstenedione into more potent androgen testosterone. The 17 β -HSD enzyme may represent a regulatory point in androgen and estrogen metabolism within the skin [22].

Also the skin and sebaceous gland are capable of synthesizing cholesterol denovo from acetate [23] [24]. Although this cholesterol is utilized in cell membranes, in the formation of the epidermal barrier, and is secreted in sebum, it is used, as a substrate for steroid hormone synthesis had not been established until recently. In order for steroid synthesis to occur, cholesterol needs to be translocated from the outer to the inner mitochondrial membrane. This process is regulated by the steroidogenic acute regulatory protein. [25]

Another factor will contribute to the above biochemical change that when the sebaceous gland produces sebum and this enhances the skin regeneration rate (as well as the death rate of existing skin cells). The increased number of dead skin cells gets deposited in the hair follicles of the skin (the skin also produces more oil and becomes sticky, thus aiding the depositing process). This also attracts bacteria, which make it their home. This leads to the skin openings getting clogged and as a result, pimples are formed [26]. And this entire exercise gets started due to an increase in the production of hormones. Thus it is referred to as hormonal acne.

Most women who have a hormonal component to their acne have normal levels of serum androgen as in our study in mild acne vulgaris group, because cases of hormonal acne are related to increased local or peripheral production of androgens, usually at the site of the sebaceous gland. Routine hormonal work-up, therefore, is not usually necessary in an adult woman with acne [27].

The present study agrees with the study of Bernard M, [25] who found that increase in androgen level including testosterone

LH, FSH & LH/FSH Ratio

The mean serum level of LH, FSH and LH/FSH ratio has shown no significant difference in female patient with acne vulgaris in compared with control group as shown in table (3). But the value of ratio LH/FSH was significantly higher in severe acne female patients by comparison with control group, while there was no significant differences in female with mild and moderate acne when it compared with control group as shown in table (4).

In all women or children with acne the possibility of a hyperandrogenic state should be considered. In the former, the presence of irregular menses and hirsutism increases the likelihood of finding clinically significant hyperandrogenism. Additionally, gynecologic endocrine evaluation may be indicated in women who have acne resistant to conventional therapy, who relapse quickly after a course of isotretinoin, or in whom there is a sudden onset of severe acne[10]. This result also agrees with other study which was reported by Bernard M[22] .

In the study group, we found the increase in value of the ratio was more than two in patients with severe acne vulgaris. As we know the increase of this ratio for more than two had been considered as a “gold standard” in Polycystic ovary syndrome (PCOS) diagnosis for a long time. [29]

A diagnosis of POCS can be made on the basis of a history of irregular period and increased facial hair and severe acne. [30] So our result may help in diagnosis of PCOS depending on this ratio for these patients with severe *acne vulgaris*. Excess (LH) increases ovarian androgen secretion. Because of decreased levels of FSH related to LH, the ovarian granulosa cells cannot aromatize the androgens into estrogens [31].

TABLE-3. The Mean Serum Levels of LH, FSH & LH/FSH in Female Patients and Control

LH\FSH	Severe				moderate				mild			
	M	SD	No.	P-value	M	SD	No.	P-value	M	SD	No.	P-value
patients	2.8	0.61	10	0.01	1.75	0.46	11	0.46	1.52	0.59	14	0.50
control	1.5	1.31	22		1.5	1.31	22		1.5	1.31	22	

TABLE- 4. The Mean Serum Levels Of LH/FSH Ratio in Severe, Moderate And Mild Female Patients And Control

Female Group	LH(mlU/ml)				FSH(mlU/ml)				LH/FSH			
	M	SD	No.	P-value	M	SD	No.	P-value	M	SD	No.	P-value
patients	14.2	4.52	35	0.21	5.5	1.88	35	0.48	1.8	1.1	35	0.61
control	12.8	6.47	22		5.7	3.59	22		1.45	1.31	22	

Patients with PCOS may have a high serum testosterone level (150-200 ng/dL) or an increase in the (LH/ FSH ratio) more than 2-3, but recently American College of Obstetricians and Gynecologists (ACOG) guidelines have suggested that laboratory and imaging studies are best used to exclude a virilizing tumor. The diagnosis of PCOS is made clinically by the presence of an ovulation (fewer than nine periods per year or periods > 40 days apart) and signs of hyperandrogenism[3].

We suggest from our investigation and previous studies that an increase LH / FSH ratio was considered as a predisposing factor for the diagnosis of PCOS.

CONCLUSION

1. Acne vulgaris is associated with disorder of androgens hormone .
2. Acne vulgaris is an indicator to androgens levels changes.
3. The evaluation of LH/FSH Ratio in patient with severe acne may help to diagnosis PCOS.

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